

ADVANCED ORGANIC CHEMISTRY

REACTIONS,
MECHANISMS, AND
STRUCTURE

FOURTH EDITION

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the carbonyl group, and the rate increases because moving the double bond from the 7 to the 6 position causes a change in conformation at the carbonyl group (the difference in the side chain at C-17 does not affect the rate).

Quantitative Treatments of the Effect of Structure on Reactivity¹⁵

Suppose a reaction is performed on a substrate molecule that can be represented as XGY, where Y is the site of the reaction, X a variable substituent, and G a skeleton group to which X and Y are attached, and we find that changing X from H to CH₃ results in a rate increase by a factor, say, 10. We would like to know just what part of the increase is due to each of the effects previously mentioned. The obvious way to approach such a problem is to try to find compounds in which one or two of the factors are absent or at least negligible. This is not easy to do acceptably because factors that seem negligible to one investigator do not always appear so to another. The first attempt to give numerical values was that of Hammett.¹⁶ For the cases of *m*- and *p*-XC₆H₄Y, Hammett set up the equation

$$\log \frac{k}{k_0} = \sigma \rho$$

where k_0 is the rate constant or equilibrium constant for X = H, k is the constant for the group X, ρ is a constant for a given reaction under a given set of conditions, and σ is a constant characteristic of the group X. The equation is called the *Hammett equation*.

The value of ρ was set at 1.00 for ionization of XC₆H₄COOH in water at 25°C. σ_m and σ_p values were then calculated for each group (for a group X, σ is different for the meta and para positions). Once a set of σ values was obtained, ρ values could be obtained for other reactions from the rates of just two X-substituted compounds, if the σ values of the X groups were known (in practice, at least four well-spaced values are used to calculate ρ because of experimental error and because the treatment is not exact). With the ρ value thus calculated and the known σ values for other groups, rates can be predicted for reactions that have not yet been run.

The σ values are numbers that sum up the total electrical effects (resonance plus field) of a group X when attached to a benzene ring. The treatment usually fails for the ortho position. The Hammett treatment has been applied to many reactions and to many functional groups and correlates quite well an enormous amount of data. Jaffé's review article¹⁶ lists ρ values for 204 reactions,¹⁷ many of which have different ρ values for different conditions.

¹⁵For monographs, see Exner *Correlation Analysis of Chemical Data*; Plenum, New York, 1968; Johnson *The Hammett Equation*; Cambridge University Press; Cambridge, 1973; Shorter *Correlation Analysis of Organic Reactivity*; Wiley, New York, 1982; *Correlation Analysis in Organic Chemistry*; Clarendon Press; Oxford, 1973; Chapman; *Shorter Correlation Analysis in Chemistry: Recent Advances*; Plenum, New York, 1978; *Advances in Linear Free Energy Relationships*; Plenum, New York, 1972; Wells *Linear Free Energy Relationships*; Academic Press; New York, 1968. For reviews, see Connors *Chemical Kinetics*; VCH; New York, 1990, pp. 311-303; Lewis, in Bernasconi *Investigation of Rates and Mechanisms of Reactions* (vol. 6 of Weissberger *Techniques of Chemistry*), 4th ed.; Wiley; New York, 1986, pp. 571-801; Hammett, Ref. 2, pp. 347-396; Jones *Physical and Mechanistic Organic Chemistry*, 2nd ed.; Cambridge University Press, Cambridge, 1984, pp. 36-68; Charton, *CHEMTECH* 1974, 302-311, 1975, 243-256; Hine *Structural Effects in Organic Chemistry*; Wiley; New York, 1975, pp. 55-102; Adamas's *Revs. Chem. Rev.* 1971, 41, 216-232; Laurence; Wojtkowski *Ann. Chim. (Paris)* 1978, [14] 3, 163-191. For a historical perspective, see Grunwald *CHEMTECH* 1984, 692.

¹⁶For a review, see Jaffé *Chem. Rev.* 1953, 53, 191.

¹⁷Additional ρ values are given in Wells *Chem. Rev.* 1963, 63, 171-218 and van Bekkum, Verklein; *Neyster Recl. Trav. Chim. Pays-Bas* 1959, 76, 821-827.

double bond from the 7 to 8 group (the difference in the

activity)¹⁵

he represented as XGY, and G a skeleton group to H to CH₃ results in a rate part of the increase is due to approach such a problem absent or at least negligible, negligible to one investigator merical values was that of the equation.

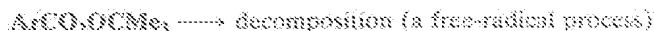
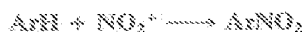
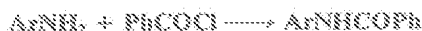
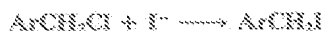
I, k is the constant for the of conditions, and σ is a e Hammett equation. I in water at 25°C. σ_m and σ is different for the meta lues could be obtained for inds, if the σ values of the es are used to calculate ρ t exact). With the ρ value t be predicted for reactions

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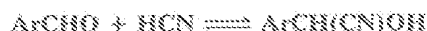
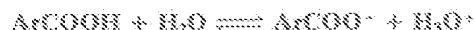
ic New York, 1988; Johnson *The ion Analysis of Organic Reactivity*; Oxford, 1973; Chapman; Shorter *Advances in Linear Free Energy Academic Press*; New York, 1968, Lewis, in Bernasconi *Investigation* try), 4th ed.; Wiley: New York, *itic Organic Chemistry*, 2nd ed.; 974, 502-511, 1975, 245-255; Hine *ss'er Russ. Chem. Rev.* 1971, 40, torical perspective, see Grunwald

Among them are reactions as disparate as the following:

Rate constants for



Equilibrium constants for



The Hammett equation has also been shown to apply to many physical measurements, including ir frequencies and nmr chemical shifts.¹⁸ The treatment is reasonably successful whether the substrates are attacked by electrophilic, nucleophilic, or free-radical reagents, the important thing being that the mechanism be the same *within* a given reaction series.

However, there are many reactions that do not fit the treatment. These are mostly reactions where the attack is directly on the ring and where the X group can enter into direct resonance interaction with the reaction site in the transition state (that is, the substrate is XY rather than XGY). For these cases, two new sets of σ values have been devised: σ' values (proposed by H. C. Brown) for cases in which an electron-donating group interacts with a developing positive charge in the transition state (this includes the important case of electrophilic aromatic substitutions; see Chapter 11), and σ'' values, where electron-withdrawing groups interact with a developing negative charge. Table 9.4 gives σ , σ' , and σ'' values for some common X groups.¹⁹ As shown in the table, σ is not very different from σ' for most electron-withdrawing groups. σ_m'' values are not shown in the table, since they are essentially the same as the σ_m values.

A positive value of σ indicates an electron-withdrawing group and a negative value an electron-donating group. The constant ρ measures the susceptibility of the reaction to electrical effects.²⁰ Reactions with a positive ρ are helped by electron-withdrawing groups and vice versa. The following ρ values for the ionization of some carboxylic acids illustrate this:²¹

$\text{XC}_6\text{H}_4\text{---COOH}$	1.00	$\text{XC}_6\text{H}_4\text{---CH=CH---COOH}$	0.47
$\text{XC}_6\text{H}_4\text{---CH}_2\text{---COOH}$	0.49	$\text{XC}_6\text{H}_4\text{---CH}_2\text{CH}_2\text{---COOH}$	0.21

¹⁵For a review of Hammett treatment of nmr chemical shifts, see Ewing, in Chapman; Shorter *Correlation Analysis in Chemistry: Recent Advances*; Plenum, New York, 1978, pp. 357-396.

¹⁶Unless otherwise noted, σ values are from Exner, in Chapman; Shorter, Ref. 18, pp. 439-540, and σ' values from Okamoto; Inakai; Brown *J. Am. Chem. Soc.* 1958, 80, 4969 and Brown; Okamoto *J. Am. Chem. Soc.* 1958, 80, 4979. σ'' values, except as noted, are from Jaffé, Ref. 16. Exner, pp. 439-540, has extensive tables giving values for more than 300 groups, as well as σ' , σ'' , σ_1 , σ_2 , and E_s values for many of these groups. Other large tables of the various sigma values are found in Hansch; Leo; Taft *Chem. Rev.* 1991, 91, 165-195. For tables of σ_p , σ_m , σ' , σ_1 , and σ_2 values of many groups containing Si, Ge, Sn, and Pb atoms, see Egorochkin; Razuvaev *Russ. Chem. Rev.* 1987, 56, 846-858. For values for heteroaromatic groups, see Mamaev; Shkurko; Baram *Adv. Heterocycl. Chem.* 1987, 42, 1-82.

¹⁷For discussions of the precise significance of ρ , see Dubois; Russen; Argile *J. Am. Chem. Soc.* 1984, 106, 4840; Ruasse; Argile; Dubois *J. Am. Chem. Soc.* 1984, 106, 4845; Lee; Shim; Chung; Kim; Lee *J. Chem. Soc., Perkin Trans. 2* 1988, 1919.

¹⁸Jones, Ref. 18, p. 42.

TABLE 8.4 σ , σ^+ , and σ^- values for some common groups¹⁸

Group	σ_p	σ_m	σ_p^+	σ_m^+	σ_p^-
O ⁻	-0.81 ¹³	-0.47 ¹¹	-4.27 ²³	-1.15 ¹²	
NMe ₂	-0.63	-0.30	-1.7		
NH ₂	-0.57	-0.09	-1.3	-0.16	
OH	-0.38 ²¹	0.13 ²²	-0.92 ²³		
OMe	-0.28 ²²	0.10	-0.78	0.05	
CMe ₃	-0.15	-0.09	-0.26	-0.06	
Me	-0.14	-0.06	-0.31	-0.10 ²³	
H	0	0	0	0	0
Ph	0.05 ²²	0.05	-0.18	0 ²³	
COO ⁻	0.11 ¹³	0.02 ¹¹	-0.41 ²²	-0.10 ¹²	
F	0.15	0.34	-0.07	0.35	
Cl	0.24	0.37	0.11	0.40	
Br	0.26	0.37	0.15	0.41	
I	0.28 ²²	0.34	0.14	0.36	
N=NPh ²⁴	0.34	0.28	0.17		
COOH	0.44	0.35	0.42	0.32	0.73
COOR	0.44	0.35	0.48	0.37	0.68
COMe	0.47	0.36			0.57
CF ₃	0.53	0.46		0.57 ²⁵	
NH ₃ ⁺	0.60 ²¹	0.86 ²¹			
CN ²⁷	0.70	0.62	0.66	0.56	1.00
SO ₂ Me	0.73	0.64			
NO ₂	0.81	0.71	0.79	0.73 ²³	1.27
NMe ₄ ⁺	0.82 ²²	0.88 ²⁸	0.41	0.36	
N ₂ ⁺	1.93 ²⁹	1.65 ²⁹	1.88 ²⁷		3 ³⁰

This example shows that the insertion of a CH₂ or a CH=CH group diminishes electrical effects to about the same extent, while a CH₂CH₂ group diminishes them much more. A ρ greater than 1 would mean that the reaction is more sensitive to electrical effects than is the ionization of XC₆H₄COOH ($\rho = 1.00$).

Similar calculations have been made for compounds with two groups X and X' on one ring, where the σ values are sometimes additive and sometimes not,²³ for other ring systems such as naphthalene²⁴ and heterocyclic rings,²⁵ and for ethylenic and acetylenic systems.²⁶

¹⁸Maruti; Ko; Hepler *Can. J. Chem.* 1974, 52, 2006.

¹⁹de la Mare; Newman *Tetrahedron Lett.* 1953, 1305 give this value as -1.6.

²⁰Amin; Taylor *Tetrahedron Lett.* 1978, 267.

²¹Sjöström; Wold *Chem. Scr.* 1976, 9, 200.

²²Byrne; Happer; Hartshorn; Powell *J. Chem. Soc., Perkin Trans. 2* 1987, 1649.

²³For a review of directing and activating effects of C=O, C=C, C=N, and C=S groups, see Charton, in Patai *The Chemistry of Double-bonded Functional Groups*, vol. 2, pt. 1; Wiley: New York, 1969, pp. 239-298.

²⁴For a review of directing and activating effects of CN and C=O groups, see Charton, in Patai; Rappaport *The Chemistry of Functional Groups, Supplement C*, pt. 1; Wiley: New York, 1983, pp. 269-323.

²⁵McDaniel; Brown *J. Org. Chem.* 1958, 23, 420.

²⁶Ustynyuk; Subbotin; Buchanova; Gruzdeva; Kazisyns *Doklady Akad. Nauk SSSR* 1976, 227, 375.

²⁷Lewis; Johnson *J. Am. Chem. Soc.* 1959, 81, 2070.

²⁸Hine *J. Am. Chem. Soc.* 1960, 82, 4877.

²⁹Binet; Kuzmanova; Kaneti; Juchnowski *J. Chem. Soc., Perkin Trans. 2* 1982, 1533.

³⁰Stone; Pearson *J. Org. Chem.* 1961, 26, 257.

³¹Bednars; Whittaker *J. Am. Chem. Soc.* 1959, 81, 1630; see also Wells; Ehrenson; Tait, Ref. 28.

³²For reviews, see Charton, in Chapman; Shorter, Ref. 18, pp. 175-268; Tomasi; Johnson *Adv. Heterocycl. Chem.* 1976, 20, 1-64.

³³For reviews of the application of the Hammett treatment to unsaturated systems, see Ford; Kunitzky; Topom, in Chapman; Shorter, Ref. 18, pp. 269-311; Charton *Prog. Phys. Org. Chem.* 1973, 10, 33-204.

The Hammett equation is a *linear free-energy relationship (LFER)*. This can be demonstrated as follows for the case of equilibrium constants (for rate constants a similar demonstration can be made with ΔG^\ddagger instead of ΔG°). For each reaction, where X is any group,

$$\Delta G = -RT \ln K$$

For the unsubstituted case,

$$\Delta G_0 = -RT \ln K_0$$

The Hammett equation can be rewritten

$$\log K - \log K_0 = \sigma \rho$$

so that

$$\frac{-\Delta G}{2.3RT} + \frac{\Delta G_0}{2.3RT} = \sigma \rho$$

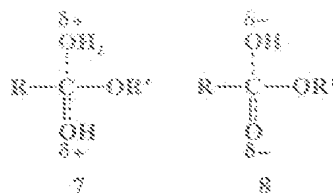
and

$$-\Delta G = \sigma \rho 2.3RT - \Delta G_0$$

For a given reaction under a given set of conditions, σ , R , T , and ΔG_0 are all constant, so that σ is linear with ΔG .

The Hammett equation is not the only LFER.³⁷ Some, like the Hammett equation, correlate structural changes in reactants, but the Grunwald-Winstein relationship (see p. 360) correlates changes in solvent and the Brønsted relation (see p. 258) relates acidity to catalysis. The Taft equation is a structure-reactivity equation that correlates only field effects.³⁸

Taft, following Ingold,³⁹ assumed that for the hydrolysis of carboxylic esters, steric and resonance effects will be the same whether the hydrolysis is catalyzed by acid or base (see the discussion of ester-hydrolysis mechanisms, reaction 0-10). Rate differences would therefore be caused only by the field effects of R and R' in RCOOR'. This is presumably a good system to use for this purpose because the transition state for acid-catalyzed hydrolysis (7) has a greater positive charge (and is hence destabilized by $-I$ and stabilized by $+I$ substituents) than the starting ester, while the transition state for base-catalyzed hydrolysis (8)



³⁷For a discussion of physicochemical preconditions for LFERs, see Finet *Prog. Phys. Org. Chem.* 1970, 11, 129-161.

³⁸For reviews of the separation of resonance and field effects, see Charton *Prog. Phys. Org. Chem.* 1981, 13, 119-251; Shorter *Q. Rev. Chem. Soc.* 1978, 24, 433-455; Chem. Rev. 1969, 5, 269-274. For a review of field and inductive effects, see Reynolds *Prog. Phys. Org. Chem.* 1983, 14, 165-203. For a review of field effects on reactivity, see Grah. *Angew. Chem. Int. Ed. Engl.* 1978, 15, 560-575 [*Angew. Chem.* 88, 623-627].

³⁹Ingold *J. Chem. Soc.* 1933b, 1032.

³⁸For another set of field-effect constants, based on a different premise, see Drahlé et al. *Bull. Soc. Chim. France*, 1976, 160-164.

σ_p'

0

0.73

0.68

0.87

1.00

1.27

3³⁰

diminishes electrical
in much more. A p
tical effects than is

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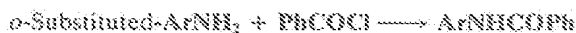
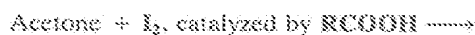
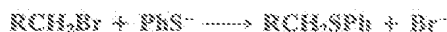
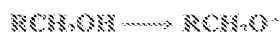
has a greater negative charge than the starting ester. Field effects of substituents X could therefore be determined by measuring the rates of acid- and base-catalyzed hydrolysis of a series XCH_2COOR' , where R' is held constant.⁴⁵ From these rate constants, a value σ_f could be determined by the equation⁴¹

$$\sigma_f = 0.181 \left[\log \left(\frac{k}{k_0} \right)_B - \log \left(\frac{k}{k_0} \right)_A \right]$$

In this equation $(k/k_0)_B$ is the rate constant for basic hydrolysis of XCH_2COOR' divided by the rate constant for basic hydrolysis of CH_3COOR' , $(k/k_0)_A$ is the similar rate-constant ratio for acid catalysis, and 0.181 is an arbitrary constant. σ_f is a substituent constant for a group X, substituted at a saturated carbon, that reflects only field effects.⁴² Once a set of σ_f values was obtained, it was found that the equation

$$\log \frac{k}{k_0} = \rho \sigma_f$$

holds for a number of reactions, among them:⁴³



As with the Hammett equation, σ_f is constant for a given reaction under a given set of conditions. For very large groups the relationship may fail because of the presence of steric effects, which are not constant. The equation also fails when X enters into resonance with the reaction center to different extents in the initial and transition states. A list of some σ_f values is given in Table 9.5.⁴⁴ The σ_f values are about what we would expect for pure field-effect values (see p. 18) and are additive, as field effects (but not resonance or steric effects) would be expected to be. Thus, in moving a group one carbon down the chain, there is a decrease by a factor of 2.8 ± 0.5 (compare the values of R and RCH_2 in Table 9.5 for R = Ph and CH_3CO). An inspection of Table 9.5 shows that σ_f values for most groups are fairly close to the σ_m values (Table 9.4) for the same groups. This is not surprising, since σ_m values would be expected to arise almost entirely from field effects, with little contribution from resonance.

Since σ_p values represent the sum of resonance and field effects, these values can be divided into resonance and field contributions if σ_f is taken to represent the field-effect

⁴¹The symbol σ_f is also used in the literature; sometimes in place of σ_r , and sometimes to indicate only the field (not the inductive) portion of the total effect (p. 17).

⁴²There is another set of values (called σ^+ values) that are also used to correlate field effects. These are related to σ_f values by $\sigma^+_{HX} = 0.45\sigma_{f(HX)}$. We discuss only σ_f , and not σ^+ values.

⁴³Wells, Ref. 17, p. 196.

⁴⁴These values are from Bromilow; Brownlee; Lopez; Taft, Ref. 52, except that the values for $NHAc$, OH , and I are from Wells; Ehrenson; Taft, Ref. 48, the values for Ph and NMe_2 are from Ref. 51 and Taft; Denot; Sclaf, Ref. 47, and the value for CMe_3 is from Both-Pauit; de Meyer-van Duyse; Tollenaere *J. Mol. Struct.* 1973, 19, 811. The values for the CH_2Ph and CH_2COCH_3 groups were calculated from σ^+ values by the formula given in footnote 42. For much larger tables of σ_f and σ_R values, see Charton, Ref. 38. See also Ref. 19 and Taylor; Wain *J. Chem. Soc., Perkin Trans. 2* 1966, 1765.

of substituents X could catalyzed hydrolysis of a te constants, a value σ_I

of XCH_2COOR divided the similar rate-constant substituent constant for a effects.⁴² Once a set of

$Ph + Br^-$

O ϕ

on under a given set of of the presence of steric ters into resonance with states. A list of some σ_I would expect for pure t not resonance or steric carbon down the chain, of R and RCH_2 in Table that σ_I values for most ps. This is not surprising, field effects, with little

cis, these values can be represent the field-effect

times to indicate only the field field effects. These are related

the values for NHAc, OH, and Ref. 51 and Taft; Deno; Skell, e *J. Mol. Struct.* 1973, 19, 811. y the formula given in footnote 19 and Taylor; Wait *J. Chem.*

TABLE 9.5 σ_I and σ_R^0 values for some groups⁴⁶

Group	σ_I	σ_R^0	Group	σ_I	σ_R^0
CMe ₃	-0.07	-0.17	OMe	0.27	-0.42
Me	-0.05	-0.13	OH	0.27	-0.44
H	0	0	I	0.39	-0.12
PhCH ₂	0.04		CF ₃	0.42	0.08
NMe ₂ ⁴⁶	0.06	-0.55	Br	0.44	-0.16
Ph	0.10	-0.10	Cl	0.46	-0.18
CH ₃ COCH ₂	0.10		F	0.50	-0.31
NH ₂	0.12	-0.50	CN	0.56	0.08
CH ₃ CO	0.20	0.16	SO ₂ Me	0.60	0.12
COOEt	0.20	0.16	NO ₂	0.65	0.15
NHAc	0.26	-0.22	NMe ₃ ⁴⁶	0.66	

portion.⁴⁷ The resonance contribution σ_R^{48} is defined as

$$\sigma_R = \sigma_P - \sigma_I$$

As it stands, however, this equation is not very useful because the σ_R value for a given group, which should be constant if the equation is to have any meaning, is actually not constant but depends on the nature of the reaction.⁴⁹ In this respect, the σ_I values are much better. Although they vary with solvent in some cases, σ_I values are essentially invariant throughout a wide variety of reaction series. However, it is possible to overcome⁵¹ the problem of varying σ_R values by using a special set of σ_R values, called σ_R^0 ,⁵¹ that measure the ability to delocalize π electrons into or out of an unperturbed or "neutral" benzene ring. Several σ_R^0 scales have been reported; the most satisfactory values are obtained from ¹³C chemical shifts of substituted benzenes.⁵² Table 9.5 lists some values of σ_R^0 , most of which were obtained in this way.⁵³

An equation such as

$$\log \frac{k}{k_0} = \rho_I \sigma_I + \rho_R \sigma_R^0$$

⁴⁶For σ_R^0 values for some other NR₂ groups, see Korzhenevskaya; Titov; Chotik; Chekhina *J. Org. Chem. USSR* 1987, 26, 1109.

⁴⁷Although we give a σ_I value for NMe₂⁴⁶, (and σ_R values for three charged groups in Table 9.6), it has been shown that charged groups (called polar substituents) cannot be included with uncharged groups (dipolar substituents) in one general scale of electrical substituent effects; Marriott; Reynolds; Topsom *J. Org. Chem.* 1982, 50, 741.

⁴⁸Roberts; Morland *J. Am. Chem. Soc.* 1953, 75, 2167; Taft *J. Am. Chem. Soc.* 1957, 79, 1043; *J. Phys. Chem.* 1960, 64, 1805; Taft; Lewis *J. Am. Chem. Soc.* 1958, 80, 2436; Taft; Deno; Skell *Annu. Rev. Phys. Chem.* 1958, 9, 287-314, pp. 290-293.

⁴⁹For reviews of the σ_I and σ_R concept as applied to benzenes and naphthalenes, respectively, see Ehrenson; Brownlee; Taft *Prog. Phys. Org. Chem.* 1973, 10, 1-80; Wells; Ehrenson; Taft *Prog. Phys. Org. Chem.* 1968, 6, 147-322. See also Taft; Topsom *Prog. Phys. Org. Chem.* 1987, 16, 1-83; Charton *Prog. Phys. Org. Chem.* 1987, 16, 287-315.

⁵⁰Taft; Lewis *J. Am. Chem. Soc.* 1959, 81, 5343; Reynolds; Dais; MacIntyre; Topsom; Marriott; von Nagy-Pelsobuki; Taft *J. Am. Chem. Soc.* 1983, 105, 378.

⁵¹For a different way of overcoming this problem, see Happer; Wright *J. Chem. Soc., Perkin Trans. 2* 1979, 694.

⁵²Taft; Ehrenson; Lewis; Glick *J. Am. Chem. Soc.* 1959, 81, 5352.

⁵³Bromilow; Brownlee; Lopez; Taft *J. Org. Chem.* 1979, 44, 4766. See also Marriott; Topsom *J. Chem. Soc., Perkin Trans. 2* 1983, 1045.

⁵⁴For a set of σ_R values for use in XY⁺ systems, see Charton *Mol. Struct. Energ.* 1987, 4, 271-317.

which treats resonance and field effects separately, is known as a *dual substituent parameter equation*.⁵⁴

The only groups in Table 9.5 with negative values of σ_f are the alkyl groups methyl and *t*-butyl. There has been some controversy on this point.⁵⁵ One opinion is that σ_f values decrease in the series methyl, ethyl, isopropyl, *t*-butyl (respectively, -0.046 , -0.057 , -0.065 , -0.074).⁵⁶ Other evidence, however, has led to the belief that all alkyl groups have approximately the same field effect and that the σ_f values are invalid as a measure of the intrinsic field effects of alkyl groups.⁵⁷

Another attempt to divide σ values into resonance and field contributions⁵⁸ is that of Swain and Lupton, who have shown that the large number of sets of σ values (σ_m , σ_p , σ_p^- , σ_p^+ , σ_f , σ_R , etc., as well as others we have not mentioned) are not entirely independent and that linear combinations of two sets of new values F (which expresses the field-effect contribution) and R (the resonance contribution) satisfactorily express 43 sets of values.⁵⁹ Each set is expressed as

$$\sigma = fF + rR$$

where f and r are weighting factors. Some F and R values for common groups are given in Table 9.6.⁶⁰ From the calculated values of f and r , Swain and Lupton calculated that the

TABLE 9.6 F and R values for some groups⁶⁰

Group	F	R	Group	F	R
COO ⁻	-0.27	0.40	OMe	0.54	-1.68
Me ₃ C	-0.11	-0.29	CF ₃	0.64	0.76
Et	-0.02	-0.44	I	0.65	-0.12
Me	-0.01	-0.41	Br	0.72	-0.18
H	0	0	Cl	0.72	-0.24
Ph	0.25	-0.37	F	0.74	-0.60
NH ₂	0.38	-2.52	NHCOCH ₃	0.77	-1.43
COOH	0.44	0.66	CN	0.90	0.71
OH	0.46	-1.89	NMe ₃ ⁺	1.54	
COOEt	0.47	0.67	N ₂ ⁺	2.36	2.81
COCH ₃	0.50	0.90			

⁵⁴There are also three-parameter equations. See, for example de Ligny and van Houwelingen *J. Chem. Soc., Perkin Trans. 2* 1987, 559.

⁵⁵For a discussion, see Shorter, in Chapman; Shorter *Advances in Linear Free Energy Relationships*, Ref. 15, pp. 98-103.

⁵⁶For support for this point of view, see Levitt; Widing *Prog. Phys. Org. Chem.* 1976, 12, 119-157; Taft; Levitt *J. Org. Chem.* 1977, 42, 916; MacPhee; Dubois *Tetrahedron Lett.* 1978, 2225; Screttas *J. Org. Chem.* 1979, 44, 3332; Hanson *J. Chem. Soc., Perkin Trans. 2* 1984, 101.

⁵⁷For support for this point of view, see, for example, Blachin *J. Phys. Chem.* 1961, 65, 2091; Bordwell; Drucker; McCollum *J. Org. Chem.* 1976, 41, 2786; Bordwell; Fried *Tetrahedron Lett.* 1977, 1121; Charton *J. Am. Chem. Soc.* 1977, 99, 5687; *J. Org. Chem.* 1979, 44, 903; Adcock; Khor *J. Org. Chem.* 1978, 43, 1272; DeYus *J. Org. Chem.* 1980, 45, 5166; *J. Am. Chem. Soc.* 1980, 102, 7988.

⁵⁸Yukawa and Tsuno have still another approach, also involving dual parameters. Yukawa; Tsuno *Bull. Chem. Soc. Jpn.* 1959, 32, 971. For a review and critique of this method, see Shorter, in Chapman; Shorter, Ref. 18, pp. 119-173, pp. 136-144. This article also discusses the Swain-Lupton and Taft σ_f , σ_p approaches. For yet other approaches, see Alinas'ev *J. Org. Chem. USSR* 1981, 17, 573; *J. Chem. Soc., Perkin Trans. 2* 1984, 1989; Ponoc Coll. Czech. Chem. Commun. 1983, 48, 1564.

⁵⁹Swain; Lupton *J. Am. Chem. Soc.* 1968, 90, 4328; Swain; Unger; Rosenquist; Swain *J. Am. Chem. Soc.* 1983, 105, 492.

⁶⁰Taken from a much longer list in Swain; Unger; Rosenquist; Swain, Ref. 59. Long tables of R and F values are also given in Hansch; Leo; Taft, Ref. 19.

4 substituent parameter

alkyl groups methyl and inion is that σ_f values are, -0.046 , -0.057 , that all alkyl groups are valid as a measure of

contributions⁶² is that of σ values (σ_m , σ_p , σ_p^+), entirely independent presses the field-effect as 43 sets of values.⁷³

ion groups are given in ton calculated that the

importance of resonance, % R , is 20% for σ_m , 38% for σ_p , and 62% for σ_p^+ .⁶¹ This is another dual substituent parameter approach.

Taft was also able to isolate steric effects.⁶² For the acid-catalyzed hydrolysis of esters in aqueous acetone, $\log (k/k_0)$ was shown to be insensitive to polar effects.⁶³ In cases where resonance interaction was absent, this value was proportional only to steric effects (and any others⁶⁴ that are not field or resonance). The equation is

$$\log \frac{k}{k_0} = E_s$$

Some E_s values are given in Table 9.7,⁶⁵ where hydrogen is taken as standard, with a value of 0.⁶⁶ This treatment is more restricted than those previously discussed, since it requires more assumptions, but the E_s values are approximately in order of the size of the groups. Charton has shown that E_s values for substituents of types CH_2X , CHX_2 , and CX_3 are linear functions of the van der Waals radii for these groups.⁶⁷

Two other steric parameters are independent of any kinetic data. Charton's v values are derived from van der Waals radii,⁶⁸ and Meyer's V^* values from the volume of the portion of the substituent that is within 0.3 nm of the reaction center.⁶⁹ The V^* values are obtained by molecular mechanics calculations based on the structure of the molecule. Table 9.7 gives v and V^* values for some groups.⁷⁰ As can be seen in the table, there is a fair, but not

TABLE 9.7 E_s , v , and V^* values for some groups⁶⁶

Group	E_s	v	$V^* \times 10^3$	Group	E_s	v	$V^* \times 10^3$
H	0	0		Cyclohexyl	-2.03	0.87	6.25
F	-0.46	0.27	1.22	iso-Bu	-2.17	0.98	5.26
CN	-0.51			sec-Bu	-2.37	1.02	6.21
OH	-0.55			CF ₃	-2.4	0.91	3.54
OMe	-0.55		3.39	t-Bu	-2.78	1.24	7.16
NH ₂	-0.61			NMe ₃ ⁺	-2.84		
Cl	-0.97	0.55	2.54	Neopentyl	-2.98	1.34	5.75
Me	-1.24	0.52	2.84	CCl ₃	-3.3	1.38	6.43
Et	-1.31	0.56	4.31	CH ₂ Br	-3.67	1.56	7.29
i	-1.4	0.78	4.08	(Me ₂ CCH ₂) ₂ CH	-4.42	2.03	
Pr	-1.6	0.68	4.78	Et ₃ C	-5.04	2.38	
iso-Pr	-1.71	0.76	5.74	Ph ₃ C	-5.92	2.92	

⁶¹The Swain-Lupton treatment has been criticized by Reynolds, *Topson J. Org. Chem.* 1984, 49, 1989; Hoehnagel; Oosterbeek; Wepster *J. Org. Chem.* 1984, 49, 1993; and Charton *J. Org. Chem.* 1984, 49, 1997. For a reply to these criticisms, see Swain *J. Org. Chem.* 1984, 49, 2005. A study of the rates of dediazotization reactions (3-23) was more in accord with the Taft and Charton (Ref. 38) σ_f and σ_R values than with the Swain-Lupton F and R values; Nakazumi; Kitao; Zollinger *J. Org. Chem.* 1987, 52, 2825.

⁶²For reviews of quantitative treatments of steric effects, see Gallo; Roussel; Berg *Adv. Heterocycl. Chem.* 1968, 43, 173-299; Gallo *Prog. Phys. Org. Chem.* 1983, 14, 115-163; Unger; Hansch *Prog. Phys. Org. Chem.* 1976, 12, 91-118.

⁶³Another reaction used for the quantitative measurement of steric effects is the aminolysis of esters (0-55); De Tar; Delahunty *J. Am. Chem. Soc.* 1983, 105, 2734.

⁶⁴It has been shown that E_s values include solvation effects; McClelland; Steenken *J. Am. Chem. Soc.* 1988, 110, 5860.

⁶⁵ E_s , v , and V^* values are taken from longer tables in respectively, Ref. 62, Charton *J. Am. Chem. Soc.* 1975, 97, 1552; *J. Org. Chem.* 1976, 41, 2217; and Ref. 69.

⁶⁶In Taft's original work, Me was given the value 0. The E_s values in Table 9.7 can be converted to the original values by adding 1.24.

⁶⁷Charton *J. Am. Chem. Soc.* 1969, 91, 613.

⁶⁸Charton, Ref. 65. See also Charton *J. Org. Chem.* 1978, 43, 3975; Idoux; Schreck *J. Org. Chem.* 1978, 43, 4002.

⁶⁹Meyer *J. Chem. Soc., Perkin Trans. 2* 1966, 1567.

⁷⁰For a discussion of the various steric parameters, see DeTar, Ref. 57.

Houwelingen *J. Chem. Soc.*,

v Relationships. Ref. 15, pp.

76, 12, 119-157; Taft; Levitt
J. Org. Chem. 1979, 44, 3332;

65, 2001; Bordwell; Drucker;
Charton *J. Am. Chem. Soc.*
1272; DeTar *J. Org. Chem.*

Yukawa; Tsuno *Bull. Chem.*
ipman; Shorter. Ref. 18, pp.
ses. For yet other approaches,
84, 1589; Ponce *Coll. Czech.*

sin *J. Am. Chem. Soc.* 1983,

g tables of R and F values are

perfect, correlation among the E_s , v , and V^* values. Other sets of steric values, e.g., E_s^* ,⁷¹ E_s^* ,⁷² Ω_s ,⁷³ and ζ_s ,⁷⁴ have also been proposed.⁷⁰

Since the Hammett equation has been so successful in the treatment of the effects of groups in the meta and para positions, it is not surprising that attempts have been made to apply it to ortho positions also.⁷⁵ The effect on a reaction rate or equilibrium constant of a group in the ortho position is called the *ortho effect*.⁷⁶ Despite the many attempts made to quantify ortho effects, so far no set of values commands general agreement. However, the Hammett treatment is successful for ortho compounds when the group Y in $o\text{-XC}_6\text{H}_4\text{Y}$ is separated from the ring; e.g., ionization constants of $o\text{-XC}_6\text{H}_4\text{OCH}_2\text{COOH}$ can be successfully correlated.⁷⁷

Linear free-energy relationships can have mechanistic implications. If $\log(k/k_0)$ is linear with the appropriate σ , it is likely that the same mechanism operates throughout the series. If not, a smooth curve usually indicates a gradual change in mechanism, while a pair of intersecting straight lines indicates an abrupt change,⁷⁸ though nonlinear plots can also be due to other causes, such as complications arising from side reactions. If a reaction series follows σ^+ or σ^- better than σ it generally means that there is extensive resonance interaction in the transition state.⁷⁹

Information can also be obtained from the magnitude and sign of ρ . For example, a strongly negative ρ value indicates a large electron demand at the reaction center, from which it may be concluded that a highly electron-deficient center, perhaps an incipient carbocation, is involved. Conversely, a positive ρ value is associated with a developing negative charge in the transition state.⁸⁰ The $\sigma\rho$ relationship even applies to free-radical reactions, because free radicals can have some polar character (p. 679), though ρ values here are usually small (less than about 1.5) whether positive or negative. Reactions involving cyclic transition states (p. 206) also exhibit very small ρ values.

⁷¹MacPhee; Panaye; Dubois *Tetrahedron* 1978, 34, 3553; *J. Org. Chem.* 1980, 45, 1164; Dubois; MacPhee; Panaye *Tetrahedron Lett.* 1978, 4099; *Tetrahedron* 1980, 36, 919. See also Datta; Sharma *J. Chem. Res. (S)* 1987, 422.

⁷²Fellous; Luft *J. Am. Chem. Soc.* 1973, 95, 5593.

⁷³Komatsu; Sakakibara; Hirota *Tetrahedron Lett.* 1989, 30, 3309; *Chem. Lett.* 1990, 1913.

⁷⁴Backhaus *Angew. Chem. Int. Ed. Engl.* 1978, 17, 503 [*Angew. Chem.* 90, 653].

⁷⁵For reviews, see Fujita; Nishioka *Prog. Phys. Org. Chem.* 1976, 12, 49-89; Charton *Prog. Phys. Org. Chem.* 1971, 8, 235-317; Shorter, *Ref. 55*, pp. 103-110. See also Segura *J. Org. Chem.* 1985, 50, 1045; Robinson; Horton; Foshad; Jones; Hanessian; Slater *J. Org. Chem.* 1986, 51, 3535.

⁷⁶This is not the same as the ortho effect discussed on p. 514.

⁷⁷Charton *Can. J. Chem.* 1966, 44, 2493.

⁷⁸For a discussion, see Schreck *J. Chem. Educ.* 1971, 48, 103-107.

⁷⁹See, however, Gansley *J. Org. Chem.* 1981, 46, 4595.

⁸⁰For another method of determining transition state charge, see Williams *Acc. Chem. Res.* 1984, 17, 425-430.